

REMARKS/ARGUMENTS

After entry of this paper, claims 2-7, 9, 14, and 44-55 are pending. Claims 12-13 are cancelled in an effort to place the application in condition for allowance. Claims 4, 9, and 14 are amended to place the application in condition for allowance and do not add new matter.

Claims 44-55 are added and recite certain embodiments of the previously pending claims. Support for these amendments is found throughout the specification (page 4, line 7 through page 7, line 21; page 21, lines 1-17; page 33, lines 7-16; page 34, lines 4-7; and page 37, lines 30-31) and the original claims. These new claims do not add new matter.

35 USC § 103(a) Rejection

Claims 2-7, 9, and 12-14 are rejected under this section over US Patent Nos. 6,355,648 ('648) and 6,331,562 ('562).

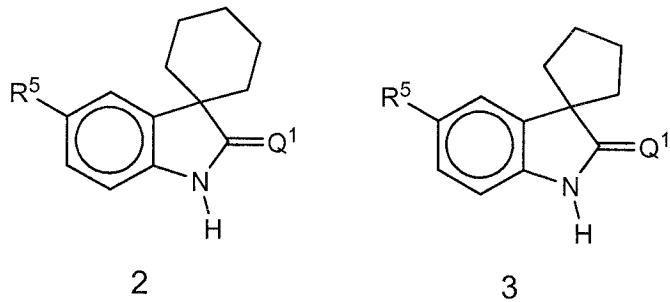
The Examiner asserted that it would have been obvious to employ both of the compounds of '648 and '562 in a method of inducing contraception and that concomitantly employing two agents, which are known to be useful for contraception individually, in a method useful for the very same purpose, is obvious.

Applicants respectfully request reconsideration and withdrawal of this rejection for the following reasons.

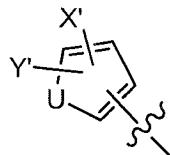
The cancellation of claims 12-13 renders the outstanding rejection moot as applied to these claims.

The amended and new claims are drawn to compounds which require that the 5-position of the indolin-2-thione be substituted with a 5-membered heterocyclic group containing one CN substituent. The compounds also must contain a H-atom at the 1, 4, 6, and 7-positions and a 5- or 6-membered spirocyclic ring at the 3-position of the indolin-2-thione backbone.

As the Examiner noted¹, '648 discusses the following compounds 2 and 3 in cols. 9-10.



R₅ of these compounds 2 and 3 of '648 may be the following group:



wherein: $U = O, S, \text{ or } NR_6$

$R_6 = H, C_1$ to C_3 alkyl, or C_1 to C_4 CO_2 alkyl

X' = halogen, CN, NO_2 , CONH_2 , CSNH_2 , CONHalkyl , CSNHalkyl , CONalkyl_2 , CSNalkyl_2 , C_1 to C_3 alkyl, or C_1 to C_3 alkoxy

Y' = H, F or C₁ to C₄ alkyl

In view of the combined large number of substituents for R₆, X', and Y', compounds 2 and 3 of '648 cover a substantial number of compounds. No combination of '648 with '562 suggests the compounds of formula (I) recited in the pending claims of the present application in combination with selective estrogen receptor modulators (SERM). Absent this suggestion in the art, only the improper use of hindsight can explain this rejection.

In addition to '648 and '562 together lacking a suggestion to utilize the claimed compounds in combination with SERMs, the compounds of formula (I) of the pending claims have a potency that could not have been ascertained or anticipated by combining

¹ Page 3 of the Advisory Action dated November 13, 2007

'648 and '562. As support, Applicants point to data provided in Fensome et al., "Novel 5-Aryl-1,3-dihydro-indole-2-thiones: Potent, Orally Active Progesterone Receptor Agonists", Bioorg. & Med. Chem. Lett., 13:1317-1320 (2003) which is included in the Information Disclosure Statement filed herewith. Fensome clearly illustrates that compounds 33-38 and 40, which are encompassed by formula I of the pending claims, are good progesterone receptor agonists.

While the compounds of the currently pending claims may be dominated by the compounds of '648, specifically compounds 2 and 3, "[t]he fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness".² As the Examiner is aware, there must be a reasonable expectation of success that the claimed invention would work for its intended purpose. That expectation is lacking in the combination of '648 with '562.

In summary, the combination of the H-atoms at the 1, 4, 6, or 7-positions, the spirocyclic ring at the 4-position, and a 5-membered heterocyclic group containing a cyano substituent at the 5-position clearly results in PR modulators with agonistic activity which is not suggested by combining '648 with '562.

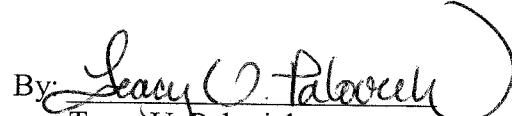
Reconsideration of this rejection is requested.

² In re Baird, 29 USPQ2d 1550, (Fed. Cir. 1994)

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account No. 08-3040.

Respectfully submitted,

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